IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Charles T. Esmon and Naomi L. Esmon

SERIAL NO: 07/730,040 ART UNIT: 182

FILING DATE: July 12, 1991 EXAMINER: P. Hutzell

FOR: MONOCLONAL ANTIBODY AGAINST PROTEIN C

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, William R. Church hereby declare that:

1. I am a Research Assistant Professor of Biochemistry at the University of Vermont. I received my Ph.D. degree from the University of Kansas Medical Center in 1979. I have conducted research in the areas of immunochemistry and blood protein chemistry for 10 years.

2. I have produced, isolated, or characterized the following monoclonal antibodies to blood proteins:

PROTEIN	NO. OF ANTIBODIES
Prothrombin	7
Factor VII	2
Factor VIII	4
Factor IX	3
Factor X	12
Factor XI	3
Protein C	4
Plasminogen	3
Tissue plasminogen activator	4
Fibrinogen	3
C4b-binding protein	2
Ceruloplasmin	2

3. Although I have isolated 4 hybridomas producing 4 monoclonals to protein C, the data, at the present time, for these antibodies support that:

(a) none of the antibodies are directed exclusively to the zymogen and do not bind activated Protein C

SERIAL NO: 07/730,040
FILING DATE: July 12, 1991
DECLARATION UNDER 37 C.F.R. §1.132

(b) none of the antibodies bind calcium ion in coordination with the small peptide epitope
(c) none appear to bind the same epitope as HPC-4

4. Based on my 10 years of experience in the field, antibody HPC-4 is a unique monoclonal antibody and it is my opinion that it would be very difficult to isolate the same hybridoma/antibody as HPC-4, even after reviewing the Stearns, et al. *J. Biol. Chem.* 263(2), 826-832 (January 15, 1988) and Esmon, N., et al. Devel. biol. Standard, vol. 67, pp 75-82 (S. Karger, ed. Basel, 1987) publications. I am not aware of any antibodies to blood coagulation proteins that block activation and require calcium for binding to the protein. Antibody HPC-4 was the first monoclonal antibody to a calcium-dependent epitope distinct from the protein regions known to bind calcium. The identification of a calcium-dependent epitope in the activation peptide of protein C was a novel observation.

5. I declare that all statements made herein of my own knowledge are true. These statements are made with the knowledge that willful false statements are punishable by fine or imprisonment under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

William R. Church

William R. Church

Date: February 3, 1992